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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/763,370

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Etsuro Ogata

OGATA4

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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1643

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/763,370	<b>Applicant(s)</b> OGATA ET AL.	
	<b>Examiner</b> Alana M. Harris, Ph.D.	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10/31/2007 & 01/31/2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-6, 8-15, 25-30 and 32-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-6, 8-15, 25-30 and 32-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Request for Continued Examination*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

2. Claims 2-6, 8-15, 25-30 and 32-36 are pending.

Claims 8 and 32 have been amended.

Claims 33-36 have been added.

Claims 2-6, 8-15, 25-30 and 32-36 are examined on the merits.

### *Withdrawn Rejections*

#### *Claim Rejections - 35 USC § 112*

3. The **NEW MATTER** rejection of claims 8-15, 25-29 under 35 U.S.C. 112, first paragraph, for including the recitations, "wherein a layer crossover index indicates amelioration of the patient's condition" and "...using at least one of a formative marker that reflects the activity of osteoblasts or at least one of a marker that reflects the activity of osteoclasts," as failing to comply with the written description requirement is withdrawn because of the amendment and deletion of the recitations, respectively.

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4. The rejection of claim 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, because the method steps read on measuring a marker for bone formation and a marker for bone resorption, ICTP is now withdrawn because of the amendment to the claim.

***Maintained Grounds of Objection***

***Specification***

5. The objection of the amendment filed May 17, 2006 and May 1, 2007 under 35 U.S.C. 132(a) because it introduces new matter into the disclosure is maintained and made.

Applicants traverse the instant objection in the Remarks filed October 31, 2007, see page 16, 1<sup>st</sup> full paragraph. Applicants respectfully remind the Examiner the instant application was originally filed in the Japanese language and the original text supports the amendment in the English language translation. Applicants conclude those arguments noting there can be no new matter given the circumstance of a mis-translation.

Moreover, a declaration under 37 CFR 1.132 by Tetsuya Aratani submitted January 31, 2008 declares a European examiner accepted the mistranslation of the definition of the Z value. Mr. Aratani furthers the declaration noting the attachment of a copy of the Communication pursuant to Article 96(2) EPC and reference a sentence in

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the Communication. These points of view and the declaration have been carefully considered, but found unpersuasive.

The Examiner reiterates original specification cites on page 9, lines 5-8, "Z value is defined by (measured value - average for the patients with bone metastasis)/(standard deviation of a patient without bone metastasis)." Applicants assert and declare that this was a mis-translation, however Applicants have not presented a declaration from a certified translator attesting to the alleged mis-translation. By all accounts Mr. Aratani does not seem to be a certified translator submitting objective evidence. Applicants are reminded the European Patent Office is a separate and distinct entity from the U.S. Patent Office and each is governed by different and distinct rules and statutes. The Examiner reviewed page 21 of 61 pages within the declaration and attachments and reiterates she cannot read the Japanese language. Consequently, one of ordinary skill in the art cannot verify whether or not the Z value did in fact use an average **without** bone metastasis. Accordingly, the objection is maintained.

***Maintained Rejections***

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. The **NEW MATTER** rejection of claims 2-6, 8-15, 25-30, 32 and new claims 33-36 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and made.

a. Applicants traverse the instant rejection based on the arguments presented in the section numbered 3 on the instant Action. Applicants further arguments asserting the Z value would not make sense as presented in the original specification, see page 9, lines 5-8, “as one would not compare patients with bone metastasis to patients without bone metastasis.”, see page 13 of the Remarks. These arguments and points of view have been carefully considered, but found unpersuasive.

As noted in the response earlier, Applicants have not presented objective evidence supporting the alleged error, a certified translator is not of record attesting the mis-translation, and the Examiner cannot read the Japanese language. Applicants point out an example, which reads on prostate cancer and cannot be extrapolated to provide support for the instant claims that broadly read on a method of diagnosing amelioration and/or exacerbation of metastasis of malignant tumor to bone in a patient with *cancer*, which includes any and every type of cancer. Moreover, the original specification cites on page 9, lines 5-8, “Z value is defined by (measured value -

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average for the patients with bone metastasis)/(standard deviation of a patient without bone metastasis). Consequently, one of ordinary skill in the art cannot verify whether or not the Z value did in fact use an average **without** bone metastasis. Accordingly, the rejection is maintained.

b. Claims 32 and 35 are regarded as containing new matter because they cite a method of evaluation the efficacy of a drug and a method of evaluating the degree of exacerbation, respectively utilizing just one marker, ICTP, a bone resorption marker. However, the specification, specifically the Examples, 1-3 does not support the implementation of this sole marker yielding information regarding the methods.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. The rejection of claims 2-6, 8-15, 25-30, 32 and new claims 33 and 34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and made.

a. Claims 6, 8 and 30 are vague and indefinite in the recitation “and determining a crossover index by dividing said Z value for osteocalcin by said Z value for ..., said crossover index and said ICTP level providing a diagnosis...”.

Applicants assert in the declaration this rejection should be overcome by the explanation given the traversal set forth in the pending new matter rejection and

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corresponding arguments. These points of view have been carefully considered, but found unpersuasive.

The information listed on page 8, line 6 of the specification does not absolve the instant rejection. The amendment to claim 8 does not resolve the indefiniteness of claims 6, 30, the instant claim and those that depend from them. The newly amended language of claim 8 is not supported by the specification as alleged by Applicants and what is listed in the specification, particularly page 10, lines 21-24 is contravene to the claim language of claim 8. Accordingly, the rejection is maintained for the reasons of record and listed herein.

b. Claims 2-6, 8-17, 25-30 and new claims 33 and 34 continue to be vague and indefinite because it is not clear from the claims how the two markers are used in ascertaining efficacy of a drug and the method steps are not clear.

Applicants assert in the declaration this rejection should be overcome by the explanation given the traversal set forth in the pending new matter rejection and corresponding arguments. Furthermore, Applicants rely on policies governing the European examiner set forth by the European Patent Office in hopes of overcoming the instant rejection. These points of view have been carefully considered, but found unpersuasive.

The Examiner has carefully reviewed the specification, particularly page 8, line 6 of the specification and notes it does not absolve the instant rejection. As stated herein and before the new matter found within the specification and claims does not support the claimed invention. The language of claim 8 is not supported by the specification as



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alleged by Applicants and what is listed in the specification and is contravene to the claim language of claim 8. Accordingly, the rejection is maintained for the reasons of record and listed herein.

c. Claim 32 continues to be vague and indefinite in the recitation “the improvement” in line 6 of the claim.

Applicants recite patents the U.S. Patent Office has allowed including Jepson language and hence withdrawal of the instant rejection is respectfully requested. These points of view have been carefully considered, but found unpersuasive.

It is still not clear what one of ordinary skill in the art is supposed to assess as improved. Applicants have now amended the claim to now cite the improvement is based solely on ICTP, whereas before it was both a marker of bone formation and a marker of bone resorption, ICTP. Furthermore, the claim does not address how the improvement comprising observing ICTP values over an undefined time demonstrating the progression of disease satisfies the evaluation of the efficacy a cancer drug, inhibition of metastasis and amelioration of metastasis. Applicants' claim continues not to be clear and definite.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 35 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Tähtelä R and Thölix E (Anticancer Res. 16(4B): 2289-93, Jul-Aug, 1996, abstract only). Tähtelä discloses a method of measuring serum concentrations of type I collagen carboxyterminal telopeptide (ICTP) in 25 patients with bone metastases, see entire abstract. S-ICTP was significantly higher in metastatic patients than in controls. Tähtelä evaluated the usefulness of this bone remodelling marker, as well as others in diagnosing and monitoring metastatic bone disease in breast cancer patients.

12. Claim 35 is rejected under 35 U.S.C. 102(b) as being anticipated by Akimoto S et al. (Jpn J Clin Oncol. 26(3):157-63, June 1996). Akimoto discloses a method of serially measuring serum levels of several markers including ICTP in 16 prostate cancer patients during treatment. The serum levels of PICP, ICTP, ALP, and PSA were significantly higher in prostate cancer patients with bone metastasis than in patients with either BPH or prostate cancer without bone metastasis, see Results section on page 158. ICTP reflects the metastatic burden in bone and is useful for monitoring the response of bone metastasis to therapy.

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13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.  
14 September 2008  
/Alana M. Harris, Ph.D./  
Primary Examiner, Art Unit 1643